00766.000043 PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	:	Examiner: Ram R. Shukla
AKIHIRO UMEZAWA, ET AL.	)	
	:	Group Art Unit: 1632
Application No.: 09/749,728	)	
	:	
Filed: December 28, 2000	)	
	:	
For: THE CELL HAVING THE POTENTIALITY OF DIFFERENTIATION INTO CARDIOMYOCYTES	)	
	:	January 13, 2005

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

THIRD SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Sir:

In compliance with the duty of disclosure under 37 C.F.R. § 1.56 and in accordance with the practice under 37 C.F.R. §§ 1.97 and 1.98, the Examiner's attention is directed to the documents listed on the enclosed Form PTO-1449. Copies of the listed documents are also enclosed.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first-class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on

January 13, 2005
(Date of Deposit)

LAWRENCE S. PERRY
(Name of Attorney for Applicant)

Signature

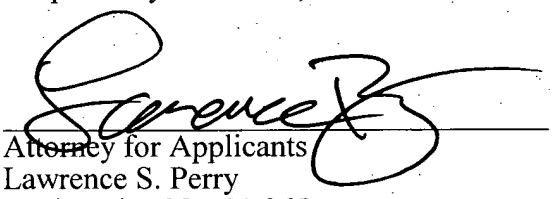
January 13, 2005
Date of Signature

It is respectfully requested that the above information be considered by the Examiner and that a copy of the enclosed Form PTO-1449 be returned indicating that such information has been considered.

We also enclose a check for the required fee of $180.00 to cover the Information Disclosure Statement under 37 C.F.R. 1.97(c)(2).

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our address given below.

Respectfully submitted,



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NY MAIN 475794v1

FORM PTO 1449 (*modified*)

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

LIST OF REFERENCES CITED BY APPLICANT(S)
(Use several sheets if necessary)

ATTY DOCKET NO.	APPLICATION NO.
00766.000043	09/749,728

APPLICANT: Akihiro Umezawa, et al.

FILING DATE	GROUP
December 28, 2000	1632

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES/NO/ OR ABSTRACT

OTHER DOCUMENT(S) (Including Author, Title, Date, Pertinent Pages, Etc.)

		Takeda, et al., "Can the life span of human marrow stromal cells be prolonged...", *The Journal of Gene Medicine*, Vol. 6 (2004), pages 833-845
		Xu, et al., "Mesenchymal Stem Cells from Adult Human Bone Marrow Differentiate into a...", *Society of Experimental Biology and Medicine*, Vol. 229 (2004) pages 623-631

EXAMINER	DATE CONSIDERED

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Claims 1-46 remain rejected under 35 U.S.C. §102 as anticipated by the art of record:

- Klug (*Journal of Clinical Investigation*, Vol. 98 (1996), pages 216-224.
- Juttermann (*Proc. Natl. Acad. Sci.*, USA, Vol 91 (1991), pages 11797-11801).
- Pinney (*Environmental Health Perspectives*, Vol. 80 (1989) pages 221-227).
- Shi (*Blood,* Vol. 92 (1998), pages 362-367).
- Young (*Proceedings of the Society of Experimental Biology and Medicine*, Vol. 221 (1999), pages 63-71).
- Makino (*Journal of Clinical Investigation*, Vol. 103 (1999), pages 697-705).

In support of the rejection, the Examiner notes that absent amending the claims to physically distinguish the prior art, it is Applicants' burden to provide evidence the present invention functionally distinguishes such references. In response, claim 1 has been amended to recite, in part, that the stem cell which differentiates into cardiomyocyte is derived from adult bone marrow. At least, this salient feature of the present invention is not taught or suggested by the prior art, as discussed below.

The stem cells of Klug et al are embryonic stem cells, but not bone marrow-derived stem cells, as now recited in the pending claims.

Juttermann et al suggest that the toxicity of a DNA methylation inhibitor such as 5-aza-2'-deoxycytidine (5-azadCyd) and 5-azacytidine (5-azaCyd) is due not to inhibition of DNA methylation, but to DNA methyltransferase (which binds to DNA substituted with the inhibitor). That is to say, Juttermann merely disclose that the demetylating agent has activity of inducing differentiation for specific cells. However,

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3/(...continued)
would be shed at the stage of the differentiation, and GFP expression would not be observed.

Juttermann does not disclose nor suggest an isolated bone marrow-derived stem cell of the present invention.

The stem cells of Pinney et al are embryonic stem cells, but not bone marrow-derived stem cells, which are used in the present invention.

Shi et al disclose that the stem cells which differentiated into endothelial cells were isolated from bone marrow. However, Shi does not disclose or suggest adult stem cells which can differentiate into a cardiomyocyte.

Young discloses that 5 populations of human mesenchymal stem cells[4/] were subjected to insulin/dexamethazone treatment so as to respectively differentiate into myotubes, adipocytes, cartilage nodule, and bone nodule, respectively. However, Young neither discloses nor suggests any cells that differentiate into a cardiomyocyte.

Finally, Makino discloses a cardimomyogenic cell line derived from bone marrow stromal cells which differentiates into only cardiomyocytes, whereas the stem cells of the present invention which can differentiate other cells in addition to cardiomyocytes.

In view of the above amendments and remarks, Applicants submit that all of the Examiner's concerns are now overcome and the claims are now in allowable condition. Accordingly, reconsideration and allowance of this application is earnestly solicited.

Claims 1, 6-19, 21-28, 38, 39, 41, 43, 44, 47-63 and 78-91 remain presented for continued prosecution.

4/ That is, (i) 25-year-old female dermal fibroblast, (ii) 22-week-old fetal male skeletal muscle cells derived from the thigh muscle, (iii) 25-week-old fetal female muscle cells derived from the triceps muscle, (iv) male and (v) female geriatric cells from skeletal muscle.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,

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